

N O T I C E

THIS DOCUMENT HAS BEEN REPRODUCED FROM
MICROFICHE. ALTHOUGH IT IS RECOGNIZED THAT
CERTAIN PORTIONS ARE ILLEGIBLE, IT IS BEING RELEASED
IN THE INTEREST OF MAKING AVAILABLE AS MUCH
INFORMATION AS POSSIBLE

CYCLIC AMP SYSTEM IN MUSCLE TISSUE DURING PROLONGED HYPOKINESIA

A. Ye. Antipenko, Yu. A. Bubeyev, B. F. Korovkin,
and N. P. Mikhaleva

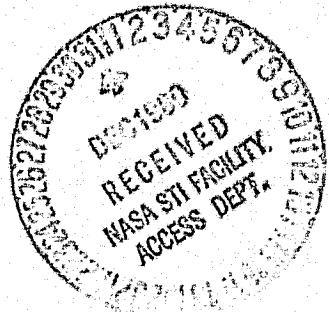
Translation of "Sistema tsAMF v myshechnoy tkani pri dlitel'noy
gipokinezii," Voprosy meditsinskoy khimii, Vol. 24, No. 6,
1978, pp. 765-768.

(NASA-TM-76186) CYCLIC AMP SYSTEM IN MUSCLE
TISSUE DURING PROLONGED HYPOKINESIA
(National Aeronautics and Space
Administration) 7 p HC A02/MF A01 CSCL 06S

N81-13627

Unclass

G3/52 29460



NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
WASHINGTON, D.C. 20546 JUNE 1980

STANDARD TITLE PAGE			
1. Report No. NASA TM - 76186	2. Government Accession No.	3. Recipient's Catalog No.	
4. Title and Subtitle CYCLIC AMP SYSTEM IN MUSCLE TISSUE DURING PROLONGED HYPOKINESIA		5. Report Date June 1980	
6. Performing Organization Code		7. Author(s) A. Ye. Antipenko, Yu. A. Bubeyev, B. F. Korovkin, and N. P. Mikhaleva Kirov Military Medical Academy, Leningrad	
8. Performing Organization Report No.		9. Performing Organization Name and Address Leo Kanner Associates Redwood City, California 94063	
10. Work Unit No.		11. Contract or Grant No. NASW-3199	
12. Sponsoring Agency Name and Address National Aeronautics and Space Administration, Washington, D.C. 20546		13. Type of Report and Period Covered Translation	
14. Sponsoring Agency Code		15. Supplementary Notes Translation of "Sistema tsAMP v myshechnoy tkani pri dilitel'noy gipokinezii," Voprosy meditsinskoy khimii, Vol. 24, No. 6, 1978, pp. 765-768.	
16. Abstract Components of the cyclic AMP system in the muscle tissue of white rats were studied during 70-75 days of hypokinesia, created by placing the animals in small booths which restricted their movements, and during the readaptation period. In the initial period, cyclic AMP levels and the activities of phosphodiesterase and adenylate cyclase in muscle tissue were increased. The values for these indices were roughly equal for controls and experimental animals during the adaptation period, but on the 70th day of the experiment cAMP levels dropped, phosphodiesterase activity increased, and the stimulative effect of epinephrine on the activity of adenylate cyclase decreased. The indices under study normalized during the readaptation period.			
(cAMP = Adenosine-3'yl-5'-monophosphate)			
17. Key Words (or(s))		18. Distribution Statement This copyrighted Soviet work is reproduced and sold by NTIS under license from VAAP, the Soviet copyright agency. No further copying is permitted without permission from VAAP.	
19. Security Classif. (of this report) Unclassified	20. Security Classif. (of this page) Unclassified	21. No. of Pages 7	22. Price

CYCLIC AMP SYSTEM IN MUSCLE TISSUE DURING PROLONGED HYPOKINESIA

A. Ye. Antipenko, Yu. A. Bubeyev, B. F. Korovkin,
and N. P. Mikhaleva

Kirov Military Medical Academy, Leningrad

(cAMP)

Components of the cyclic AMP/system in the muscle tissue of white /765* rats were studied during protracted hypokinesia (70-75 days) and during the readaptation period. It was ascertained that the level of cAMP and activities of adenyl cyclase and phosphodiesterase in muscle tissue were elevated during the initial period of motion restriction (particularly on the 5th day). Cyclic AMP content and the activities of both enzymes during the so-called adaptation period (24th to 37th days) did not materially differ from the controls. On the 70th day of the experiment, a sharp drop in cAMP level, increase in phosphodiesterase activity, /766 and decrease in the stimulative effect of epinephrine on the activity of adenyl cyclase were noted. Appreciable normalization of the indices under study occurred in the readaptation period.

The harmful effects of hypokinesia (restricted motion) on the human and animal body have been familiar to clinicians and biologists for quite some time. Protracted motor activity limitation causes decreased body mass, which, obviously, is associated to a large extent with decreased overall skeletal muscle mass. Dystrophy of parts of muscle fibers occurs, enzyme activities and the fractional makeup of muscle proteins are altered, and shifts in carbohydrate metabolism are noted [1, 2, 5]. Hence, a protracted hypokinetic state is accompanied by serious disturbances in muscle tissue metabolic processes. It has been distinctly shown in recent years that components of the cAMP system play an important role in the regulation of cell metabolism [6]. There are, however, virtually no data in the literature dealing with cAMP content and the activities of adenyl cyclase and phosphodiesterase in muscle tissue during hypokinesia. In this connection, we set out to study the status of the cAMP system in the skeletal musculature of white rats during various periods of hypokinesia and during the readaptation period.

*Numbers in the margin indicate pagination in the foreign text.

Methodology

The experiments were conducted using non-purebred white rats. Hypokinesia was created by placing the animals in special booths which restricted their movements. Muscle tissue (m. gastrocnemius) was studied during the various periods of hypokinesia (2, 5, 24, 37, and 70 days) and on the 7th day of readadaptation. White rats kept under normal vivarium conditions served as the controls. Content of cAMP was determined immunoradiologically using a prepared reagent kit from the "Amersham" company (England), and the activities of adenyl cyclase and phosphodiesterase were studied using ^3H -ATP and ^3H -cAMP isotopes, respectively, as substrates [4, 7].

Results and Discussion

767

Determinations of cAMP system components in the muscle tissue of white rats during protracted hypokinesia and in the readadaptation period are presented in the table.

As can be seen in the table, on the 2nd to 5th days of hypokinesia the activity of adenyl cyclase increased an average of 2.3 times and that of phosphodiesterase an average of 1.2 times, while the cAMP level was elevated an average of 1.9 times relative to the controls. The content of all components under study gradually decreased up to the 24th to 37th day of hypokinesia, reaching practically normal values. On the 70th day of hypokinesia the cAMP levels decreased significantly and the activity of phosphodiesterase -- an enzyme that breaks down cAMP -- increased to a statistically significant extent, while the activity of adenyl cyclase remained virtually unchanged. During the readadaptation period (data on the 7th day are shown in the table) cAMP levels and the activities of adenyl cyclase and phosphodiesterase were practically normalized.

On analyzing the data obtained, it is quite easy to see that, in the initial period of hypokinesia (particularly on the 5th day), activation of the cAMP system occurs, and then the "adaptation" period (24th to 37th days) begins and cAMP system component contents in muscle tissue

TABLE 1. CAMP CONTENT AND THE ACTIVITIES OF ADENYL CYCLASE AND PHOSPHODIESTERASE IN MUSCLE TISSUE DURING HYPOKINESIA AND IN THE READAPTATION PERIOD

Substance	Control	n	HypoKinesia						Readaptation					
			Day 2	n	Day 5	n	Day 24	n	Day 37	n	Day 70	n	Day 7	n
CAMP μ moles in 1 g tissue	238.6 \pm 38.2	26	489.2 \pm 71.4	12	692.8 \pm 53.1	15	276.8 \pm 53.1	12	333.2 \pm 35.2	12	114.0 \pm 31.2	15	276.1 \pm 62.0	12
Adenyl cyclase pmoles per protein per min.	7.81 \pm 0.55	21	11.61 \pm 0.72	12	18.04 \pm 2.60	14	9.76 \pm 1.82	12	8.74 \pm 1.04	15	9.52 \pm 0.95	12	7.59 \pm 0.90	12
Phosphodiesterase pmoles protein per minute	751.2 \pm 58.7	15	841.2 \pm 46.4	10	651.0 \pm 48.5	10	838.7 \pm 61.7	10	791.1 \pm 62.5	10	810.1 \pm 11.2	10	810.2 \pm 83.5	10

N. B.: P is calculated relative to control.

are within normal limits. On the 70th day of hypokinesia, a period of cAMP system depletion is found (cAMP levels are only 39% of normal). It should be noted that the sharp decrease in muscle tissue cAMP content on the 70th day of hypokinesia was seen upon a background of normal values for the activity of adenyl cyclase -- an enzyme participating in cAMP synthesis.

This fact compelled us to make a study of the so-called stimulated activity of adenyl cyclase during the protracted hypokinesia period. We are familiar with the fact that adenyl cyclase activity normally increases sharply when epinephrine is added to a tissue homogenate [3]. Studies we performed (see figure) showed that addition of epinephrine in concentrations of 3×10^{-4} M to homogenates of muscle tissue from the control rats led to a 2.9-fold increase in adenyl cyclase activity ($P < 0.01$), while the activity of this enzyme in homogenates of muscles from experimental rats increased only 1.4 times ($P < 0.05$) in the presence of epinephrine (70th day of hypokinesia). Consequently, qualitative shifts in the adenyl cyclase complex occur during protracted hypokinesia. There is some basis for assuming that further studies on this subject will make it possible to discover the true mechanisms of

muscle tissue metabolic disruptions during protracted hypokinesia and find ways to correct them.

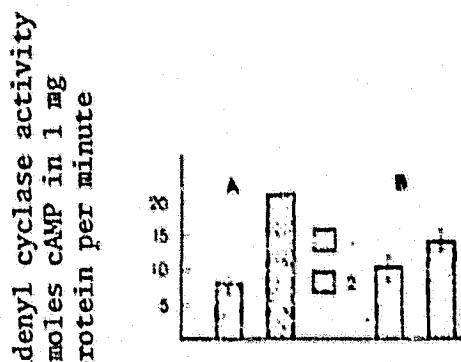


Fig. 1. The effects of epinephrine on the activity of adenyl cyclase in muscle tissue homogenates, normal conditions and during protracted hypokinesia.

1 -- without addition of epinephrine.
2 -- in the presence of epinephrine (3×10^{-4} M).
A -- control; B -- hypokinesia (70 days).

REFERENCES

1. Zhdanova, A. G., Arkh. anat., 12, 29 (1965).
2. Mikhaleva et al., Kosmicheskaya biol., 2, 42 (1970).
3. Pertseva, M. N., Uspekhi sovr. biol., 4/1, 16 (1976).
4. Tkachuk, V. A., et al., Biokhimiya, 41, 1704 (1976).
5. Chagovets, R. V., Trudy Kievsk. in-ta fizkul'tury, 2, 105 (1957).
6. Sutherland, E. W., Science, 177, 401 (1972).
7. Drummond, G. I., and L. Duncan, J. biol. Chem., 245, 976 (1970).

Copyright: Voprosy Meditsinskoy Khimii, 1978